# Is vaping an aid for smoking cessation? Review of clinical trials and international recommendations.

Ivan Berlin

Département de pharmacologie, Hôpital Pitié-Salpêtrière-Sorbonne Université, Paris

# Conflict of interest

- I declare not having received any kind of payment from the electronic cigarette or tobacco or alcohol or gaming industry
- I received honoraria for presentations at meetings in the last 3 years from Pfizer, manufacturer of varenicline.

# Haut Conseil de la santé publique/High Council of Public Health, France Avis relatif aux bénéfices-risques de la cigarette électronique

# <u>Opinion</u> on the benefits and risks of electronic cigarettes

26 Novembre 2021 published on 3 January 2022

<u>file:///C:/Users/500416/Downloads/hcspa20211126\_bnridelacileacdela</u> vdufv%20(17).pdf Request of 15 May 2020 from the General Director of Health and MILDECA to update the 2016 opinion on the benefits and risks of electronic cigarettes

 Question 1 (out of 4): Is vaping a smoking cessation aid? If so, what is its role in the smoking cessation strategy? And can vaping be considered a tobacco harm reduction tool?

# Recommendations

# The principle: to differentiate the use of ENDS in health care settings and outside it.

Consumer product *versus* medication/medical device: Evident pharmacological actions of substances delivered by a device and inhaled.

- For health care professionals : compared to therapeutic interventions overall, evidence based knowledge about their therapeutic benefit and associated risk is insufficient **at this stage** to promote their « prescription » by health care professionals. Their promotion by them is not recommended. **Justification:** Recommendation of use by health authorities must be based on in-depth assessment of benefits and risks. This involves knowledge acquisition according to international standards of study design and adverse events' data collection and reporting.
- For the general public: because of the widespread use and potential efficacy in adult smokers, a public health effectiveness cannot be excluded; a reduction in prevalence of smoking is likely.
- Pregnant smokers: because of the lack of straightforward/evidence based benefit/risk data, as always in similar cases, their use is not recommended based on the principle of *nil nocere*.

# Argument

• Statment: it is a strong hypothesis that electronic cigarettes may help smokers quit smoking as a new form of nicotine replacement therapy.

# Meta-analysis of 5 studies in Hartmann-Boyce et al. 2021b ENDS versus EDS without nicotine



Individual studies: ENDS=EDS without nicotine/placebo But RR: 1.94 (95%CI:1.21 to 3.13)

#### Footnotes

(1) 8 mg/nl arm; control group split to avoid double-counting

(2) 36 mg/nl arm; control group split to avoid double-counting

#### Analysis 3.1. Comparison 3: Nicotine EC versus non-nicotine EC, Outcome 1: Smoking cessation

	Nicotin	e EC	Non-nico	tine EC		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Bullen 2013	21	289	3	73	18.3%	1.77 [0.54 , 5.77]	
Caponnetto 2013a	22	200	4	100	20.4%	2.75 [0.97 , 7.76]	
Cobb 2021 (1)	10	130	1	65	5.1%	5.00 [0.65, 38.22]	CPS
Cobb 2021 (2)	4	130	0	65	2.5%	4.53 [0.25, 82.96]	
Eisenberg 2020	5	128	3	127	11.5%	1.65 [0.40, 6.77]	
Lucchiari 2020	13	70	11	70	42.1%	1.18 [0.57 , 2.46]	-
Total (95% CI)		947		500	100.0%	1.94 [1.21 , 3.13]	
Total events:	75		22				
Heterogeneity: Chi <sup>3</sup> = 3	3.44, df = 5 (F	e = 0.63); 1	7 = 0%			0.01	0.1 1 10 10
Test for overall effect: 2	Z = 2.74 (P =	0.006)				Favours not	n-nicotine EC Favours nicotin
Test for subgroup diffe	rences: Not a	plicable					

## Hartmann-Boyce J et al. 2022 Published after the Opinion

#### Footnotes

36 mg/mL arm; control group split to avoid double-counting
 8 mg/mL arm; control group split to avoid double-counting

# Safety: ENDS versus EDS without nicotine

# 3 studies. Bullen et al. 2013 does not provide information about SAE

	Nicoti	ne EC	Non-nico	tine EC	Malabé	Risk Ratio	Risk Ratio	2 princeps studies
Study or Subgroup	Events	Iotal	Events	Iotal	weight	M-H, Fixed, 95% Ci	M-H, Fixed, 95% CI	
3.2.1 1 week								<u>Bullen et al.</u> 2013:
Meier 2017	3	24	2	24	1.2%	1.50 [0.27 , 8.19]		arma FNDC va FDC with out pigating blinded
Subtotal (95% CI)	2	24	2	24	1.2%	1.50 [0.27 , 8.19]		-arms ENDS vs EDS without nicotine binded
Heterogeneity: Not at	plicable		2					nicating natch not blinded
Test for overall effect:	Z = 0.47 (	P = 0.64)						nicotine pateri not bindeu
								-SAE: EC-N:19.7%; EC-PI: 13.9%; NP: 11.8%
J.Z.Z 6 months Bulleo 2013	107	241	26	57	25.9%	0 97 /0 71 1 341		
Subtotal (95% CI)	101	241		57	25.9%	0.97 [0.71 , 1.34]	I	No DSMB, no Medical Dictionary for Regulatory Activities
Total events:	107		26			8 0 8	Ť	(MadDRA®) reporting
Heterogeneity: Not ap	plicable	_						(Meddra ) reporting
Test for overall effect:	Z = 0.17 (I	P = 0.87)						Eisenberg et al. 2020: "SAEs were adjudicated by an end points
3.2.3 12 weeks								
Eisenberg 2020	120	128	118	127	72.9%	1.01 [0.94 , 1.08]		evaluation committee, and the trial was monitored
Subtotal (95% CI)		128	1	127	72.9%	1.01 [0.94 , 1.08]	•	by an automal data and cafaty manitaring baard
Total events: Heterogeneity: Not ar	120 Indicable		118					by an external data and salety monitoring board,
Test for overall effect:	Z = 0.27 (I	P = 0.79)						which conferred before enrollment of the first
								which concred before enrollment of the first
Total (95% CI)		393	3	208	100.0%	1.01 [0.91 , 1.11]	+	participant and every 6 months thereafter."
Total events: Hetemospheity: Chill =	0.25 df =	2 (P = 0)	140 RR): IF = 0%	8				
Test for overall effect:	Z = 0.12 (	P = 0.91)	50), 1 - 0 A	S		Favours non-	nicotine EC Favours nicotine EC	"Serious adverse events and adverse events were
Test for subgroup diffe	erences: C	hi <sup>#</sup> = 0.26	, df = 2 (P	= 0.88), P	e = 0%			obtained via colf report at clinic and telephone follow ups"
								obtained <u>via sen-report at clinic</u> and telephone follow-ups.



# From: Effect of e-Cigarettes Plus Counseling vs Counseling Alone on Smoking Cessation: A Randomized Clinical Trial

#### JAMA. 2020;324(18):1844-1854. doi:10.1001/jama.2020.18889

	No. (%)		
	Nicotine e-cigarettes plus individual counseling (n = 128)	Nonnicotine e-cigarettes plus individual counseling (n = 127)	Individual counseling alone (n = 121)
Serious adverse events <sup>a</sup>			
Participants with a serious adverse event	1 (0.8)	4 (3.1)	2 (1.7)
Death	0	0	0
Respiratory <sup>b</sup>	1 (0.8)	0	0
Cardiovascular <sup>c</sup>	0	1 (0.8)	1 (0.8)
Neuropsychiatric	0	0	0
Other <sup>d</sup>	0	3 (2.4)	1 (0.8)
Mild adverse events		the second second	
Participants with an adverse event	120 (94)	118 (93)	88 (73)
Cough	95 (74)	81 (64)	66 (55)
Dry mouth	72 (56)	74 (58)	55 (46)
Headache	70 (55)	69 (54)	46 (38)
Rhinitis	70 (55)	67 (53)	51 (42)
Throat irritation	70 (55)	53 (42)	30 (25)
Dyspnea	53 (41)	61 (48)	43 (36)
Sore throat	44 (34)	39 (31)	21 (17)
Light headedness	42 (33)	34 (27)	28 (23)
Dizziness	39 (31)	31 (24)	37 (31)
Mouth irritation	38 (30)	24 (19)	15 (12)
Nausea	37 (29)	30 (24)	20 (17)
Indigestion	31 (24)	33 (26)	28 (23)
Mouth ulcers	19 (15)	16 (13)	7 (6)
Vertigo	16 (13)	11 (9)	9(7)

Abbreviation: e-cigarette, electronic cigarette.

<sup>a</sup> The denominator used to calculate percentages is the total number of participants randomized to each group. Only the first event for each participant in each category was counted (ie, the numbers represent the number of participants experiencing an event in each category, rather than the absolute number of events). Serious adverse events and adverse events were obtained via self-report at clinic and telephone follow-ups. All documentation obtained pertaining to each reported serious adverse event was independently evaluated by an end points evaluation committee, which determined its potential causal relationship with the study intervention.

<sup>b</sup> One participant in the nicotine e-cigarettes plus counseling group was hospitalized with a chronic obstructive pulmonary disease exacerbation secondary to pneumonia 12 days after being randomized into the trial and had used their e-cigarette in the day preceding the event. <sup>c</sup> One participant in the nonnicotine e-cigarettes plus counseling group experienced a myocardial infarction 84 days after randomization and had used their e-cigarette in the day preceding the event. One participants in the counseling alone group had critical ischemia in their left leg due to a superficial femoral artery occlusion 43 days after randomization.

<sup>d</sup> Includes 3 participants in the nonnicotine e-cigarettes plus counseling group. One participant experienced both appendicitis and a neoplastic cecal lesion during the treatment period, the second participant experienced epistaxis 39 days after randomization, and the third participant experienced noncardiac chest pain 88 days after randomization. All 3 participants had used their e-cigarette in the day preceding the events. In the counseling group, 1 participant had a urinary tract infection 16 days after randomization.

Adverse Events During the 12-Week Treatment Period by Treatment GroupAbbreviation: e-cigarette, electronic cigarette.

<sup>a</sup> The denominator used to calculate percentages is the total number of participants randomized to each group. Only the first event for each participant in each category was counted (ie, the numbers represent the number of participants experiencing an event in each category, rather than the absolute number of events). Serious adverse events and adverse events were obtained via self-report at clinic and telephone follow-ups. All documentation obtained pertaining to each reported serious adverse event was independently evaluated by an end points evaluation committee, which determined its potential causal relationship with the study intervention.

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#### From: Effect of e-Cigarettes Plus Counseling vs Counseling Alone on Smoking Cessation: A Randomized Clinical Trial.

Eisenberg et al.JAMA. 2020;324(18):1844-1854. doi:10.1001/jama.2020.18889



# ENDS versus EDS without nicotine double blind *versus* counseling only

But placebo > no intervention (Hróbjartsson A Gøtzsche PC Placebo interventions for all clinical conditions. Cochrane Database of Systematic Reviews 2010)

Unfortunately, ENDS = EDS without nicotine as in Bullen et al. 2013

Reserved.

# Comparaisons ENDS versus NRT

# Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation

EC         NRT         Risk Ratio         Risk Ratio         Risk Ratio           Study or Subgroup         Events         Total         Events         Total         Weight         M-H, Fixed, 95%, CI         M-H, Fixed, 95%, CI           Bullen 2013         21         209         17         295         27.2%         1.20 [0.65, 2.34]         Image: Comparison of the second of t		01/01/2021		Electron	nic ciganette	is for smol	oing cressat	ion - Hartmann-Boyce, J	<ul> <li>2020 ] Codhrane Library</li> </ul>
Study of Subgroup         Events         Total         Events         Total         Weight         M-H, Fixed, 95% CI           Bullen 2013         21         299         17         295         27.2%         1.26 [0.65, 2.34]           Highs 2019         79         438         44         446         70.6%         1.83 [1.30, 2.56]           Lee 2018         5         20         1         10         2.5% 2.50 [0.34, 18.63]           Total (95% CI)         747         751         100.0%         1.69 [1.25, 2.27]           Total events:         105         62           Heterogeneity: CH* 1.21, d1 = 2 (P = 0.56); P = 0%         0.01         0.1         0.1         1         100           Test for subgroup differences: Not applicable         Favours NRT         Favours EC         Favours EC		COMPANY STATES	E	0	NR	т		<b>Risk Ratio</b>	Risk Ratio
Bullen 2013       21       286       17       295       27.2%       1.26 [0.68, 2.34]         Hisjek 2019       79       438       44       446       70.6%       1.83 [1.30, 2.68]         Lee 2018       5       20       1       10       2.2%       2.50 [0.34, 18.63]         Total (95% Cl)       747       751       160.0%       1.89 [1.25, 2.27]         Total verents:       106       62         Heterogeneity: Cliff = 1.21, df = 2 (P = 0.55); P = 0.9%       0.51       0.5         Test for owaral effect: Z = 3.45 (P = 0.0005)       Favours NRT       Favours EC         Test for owaral effect: Z = 3.45 (P = 0.0005)       Favours EC       Favours EC		Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Heijek 2019     79     438     44     446     70.6%     1.83 [1.30, 2.56]       Lee 2018     5     20     1     10     2.2%     2.50 [0.34, 10.83]       Total (95% Cl)     747     751     160.0%     1.89 [1.25, 2.27]       Total overeti     106     62       Heterogeneity: Cliff = 1.21, df = 2 (P = 0.55); P = 0%     0.51     0.5       Test for overall effect: 2 = 3.46 (P = 0.0005)     Favours NRT     Favours EC		Bullen 2013	21	289	17	295	27.2%	1.26 (0.65 . 2.34)	
Lee 2018 5 20 1 10 2.2% 2.50 [0.34, 18.53] Total (98% CI) 747 751 100.0% 1.69 [1.25, 2.27] Total events: 106 62 Heterogeneity: Ch <sup>2</sup> = 1.21, df = 2 (P = 0.55); P = 0/55 Totst for subgroup differences: Not applicable Aucune comparaison en double aveugle		Hajek 2019	79	438	44	446	70.6%	1.83 (1.30 , 2.58)	
Total (95% Cl)         747         751         100.0%         1.69 [1.25, 2.27]           Total events:         105         62           Hebsroganelly: Chi <sup>2</sup> = 1.21, df = 2 (P = 0.55); P = 0/55; Tots for swall effect: 2 = 3.46 (P = 0.0005); Test for subgroup differences: Not applicable         0.51         0.51         10         100           Test for subgroup differences: Not applicable         Favours NRT         Favours EC		Lee 2018	5	20	1	10	2.2%	2.50 (0.34 , 18.63)	
Total events: 106 62 Hetsroganelly: Ch <sup>2</sup> = 1.21, df = 2 (P = 0.55); P = 0/55 Totst for swall effect: 2 = 3.46 (P = 0.0005) Test for subgroup differences: Not applicable Aucune comparaison en double aveugle		Total (95% CI)		747		751	100.0%	1.69 (1.25 . 2.27)	12
Hoterogenely: Crit® = 1.21, df = 2 (P = 0.56); P = 0% Test for overall effect; Z = 3.46 (P = 0.0005) Test for subgroup offerences: Not applicable Aucune comparaison en double aveugle		Total events:	105		62			the frank i would	×
Test for swaral effect: Z = 3.46 (P = 0.0005) Test for swaral effect: Z = 3.46 (P = 0.0005) Test for swaral effect: Z = 3.46 (P = 0.0005) Favours NRT Favours EC Aucune comparaison en double aveugle		Heterogeneity: Chi <sup>2</sup> =	1.21, df = 2	(P=0.5	5): 12 = 0%				alter als de alte
Test for subgroup offerences: Not applicable Aucune comparaison en double aveugle		Test for overall effect:	Z = 3.46 (F	= 0.000	5)				Favours NRT Envirus EC
Aucune comparaison en double aveugle		Test for subgroup diffe	rences: No	t applical	ble				3 4 F F F F F F F F F F F F F F F F F F
Aucune comparaison en double aveugle									
Aucune comparaison en double aveugle									
	Aucune compa	raison en double	aveug	le					
Hartmann, Roura, J. McRobhia, H. Lindson, N. Bullan, C. Barth R. Thaodoulou, A. Netlay,				100		Har	henanen, Re	was i McRobbie H.	Lindson N. Bullan C. Bach P. Theodoulou, A. Netlaw C.
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Database of Systematic Reviews 2020, Issue 10, Art. No.: CD010216, DOI:						Dat	abase of 3	Systematic Reviews 2	020. Issue 10. Art. No.: CD010216. DOI:
10.1002/14651858 CD010216 publ. Accessed 01 January 2021.						10.1	002/146	51858 CD010216 pub	4. Accessed 01 January 2021.

Analysis 1.1. Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation

	EC	2	NR	т		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	ABCDEI
1.1.1 Not selected on p	pregnancy							Particular States
Bullen 2013	21	289	17	295	15.7%	1.26 [0.68 , 2.34]		
Hajek 2019	79	438	44	446	40.7%	1.83 [1.30, 2.58]	-	
Lee 2018	5	20	1	10	1.2%	2.50 [0.34 , 18.63]		
Myers-Smith 2022	13	68	2	67	1.9%	6.40 [1.50 , 27.30]		
Russell 2021 (1)	34	140	15	70	18.7%	1.13 [0.66 , 1.94]	-	
Russell 2021 (2)	44	145	15	71	18.8%	1.44 [0.86 , 2.40]	<b>-</b>	22888
Subtotal (95% CI)		1100		959	97.0%	1.62 [1.29 , 2.04]	•	
Total events:	196		94				5MI	
Heterogeneity: Chi2 = 6	5.67, df = 5 (F	= 0.25); 1	F = 25%					
Test for overall effect:	Z = 4.19 (P <	0.0001)						
1.1.2 Pregnant popula	tion							
Hajek 2022 (3)	б	169	3	150	3.0%	1.78 [0.45, 6.97]		
Subtotal (95% CI)		169		150	3.0%	1.78 [0.45 , 6.97]		
Total events:	6		3					
Heterogeneity: Not app	licable							
Test for overall effect:	Z = 0.82 (P =	0.41)						
Total (95% CI)		1269		1109	100.0%	1.63 [1.30 , 2.04]	▲	
Total events:	202		97					
Heterogeneity: Chi2 = 6	5.70, df = 6 (F	= 0.35); 1	F = 10%			00	t 01 1 10 10	0
Test for overall effect:	Z = 4.27 (P <	0.0001)				0.0	Favours NRT Favours EC	0.7
Test for subgroup diffe	rences: Chi2 =	0.02, df	= 1 (P = 0.9	0), I <sup>2</sup> = 0%	6			

Hartmann-Boyce et al. 2021b

## 3 studies RR: 1.69, 95% CI 1.25 to 2.27 (ENDS > NRT)

All are open label comparisons. Treatment adherence ENDS>>NRT Only Hajek et al. 2019 shows ENDS>NRT Russel 2021 seems to be an abstract.

### Published after the Opinion

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Hartmann-Boyce J, Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews **2022**, Issue 11. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub7.

### 1.62, 95% CI 1.29 to 2.04 (ENDS > NRT)

#### New study

Pregnant smokers



#### Analysis 1.2. Comparison 1: Nicotine EC versus NRT, Outcome 2: Adverse events

### **Conclusion Cochrane Review 2022:**

"There is high-certainty evidence that ECs with nicotine increase quit rates compared to NRT and moderate-certainty evidence that they increase quit rates compared to ECs without nicotine."

### **Remarks:**

1. How is it possible that the difference is greater *versus* NRT – reference treatment – than *versus* placebo/nothing? Usually: no intervention<placebo<reference treatment ≤ new treatment (non-inferiority or superiority trials).

2. Experimental design : only two arms of two double-blind studies, the other studies and arms are open comparisons (inherent to pragmatic studies) – the preference for ENDS may explain the superiority – compliance of ENDS >> NRT.

Pragmatic trials versus double blind/double dummy RCT? AE reporting according to international standards?

#### Catherine M Pound et al. BMJ Open 2021;11:e044222

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### Published after the Opinion

#### Pooled results per outcome.

### From Ottawa, Canada

### **ENDS vs NRT**

	END	S	NRT	r .		Risk Ratio		Risk	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% CI
Bullen	21	289	17	295	20.5%	1.26 [0.68, 2.34]		8 <del>-1</del>	
Hajek	79	438	44	446	32.2%	1.83 [1.30, 2.58]			
Hatsukami	25	76	13	76	21.5%	1.92 [1.07, 3.47]			
Lee SH	16	75	21	75	22.4%	0.76 [0.43, 1.34]			-
Lee SM	5	20	1	10	3.4%	2.50 [0.34, 18.63]			•
Total (95% CI)		898		902	100.0%	1.42 [0.97, 2.09]			•
Total events	146		96						
Heterogeneity: Tau <sup>2</sup> =	= 0.09; Ch	$ni^2 = 8.$	00, df =	4 (P =	0.09); I <sup>2</sup>	= 50%	6 01	~ 1	1
Test for overall effect	z = 1.80	(P = 0)	0.07)				0.01	Favours [NRT]	Favours [E-cigarette]

# 4 études RR: 1.42, 95% CI 0.97 to 2.09 (ENDS=NRT)

#### **Smoking cessation outcome**

	ENDS NRT					Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Bullen	137	268	88	278	38.5%	1.61 [1.31, 1.99]	-		
Hajek	44	345	29	393	30.0%	1.73 [1.11, 2.70]	· · · · · · · · · · · · · · · · · · ·		
Hatsukami	19	76	22	76	27.0%	0.86 [0.51, 1.46]			
Lee SM	1	15	4	9	4.5%	0.15 [0.02, 1.14]			
Total (95% CI)		704		756	100.0%	1.25 [0.79, 1.98]	•		
Total events	201		143						
Heterogeneity: Tau <sup>2</sup> =	= 0.13; Ch	$ni^2 = 10$	0.06, df :	= 3 (P =	= 0.02); 1	$^{2} = 70\%$			
Test for overall effect	z = 0.95	5 (P = C)	).34)				Favours [NRT] Favours [ENDS]		

Consumption reduced by 50% =

Proportion of participants successfully reducing smoking consumption by 50%

		ENDS			NRT		1	Mean Difference		Mean D	Diffe	rence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	om,	95% CI	
Bullen	9.7	5.37	180	7.7	5.2	169	40.0%	2.00 [0.89, 3.11]			-		
Hatsukami	9.22	7.95	76	7.61	8.27	76	20.6%	1.61 [-0.97, 4.19]			+		
Lee SH	6.55	2.87	71	6.6	3.75	61	39.3%	-0.05 [-1.20, 1.10]			+		
Total (95% CI)			327			306	100.0%	1.11 [-0.41, 2.63]					
Heterogeneity: $Tau^2 = 1.18$ ; $Chi^2 = 6.49$ , $df = 2$ (P = 0.04); $I^2 = 69\%$									100	- 40	<u>+</u>	50	100
Test for overall effect	: Z = 1.4	13 (P =	= 0.15)						-100	Favours [NRT]	Fa	vours [ENDS]	100

#### CPD reduction =

#### Mean reduction of cigarettes from baseline

	END	S	NR	г		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl	
Bullen	107	241	96	215	43.5%	0.99 [0.81, 1.22]		1		
Hatsukami	51	69	53	72	44.7%	1.00 [0.82, 1.22]				
Lee SH	5	71	13	61	5.0%	0.33 [0.12, 0.87]				
Lee SM	11	20	4	9	6.7%	1.24 [0.54, 2.84]			-	
Total (95% CI)		401		357	100.0%	0.96 [0.76, 1.20]				
Total events	174		166							
Heterogeneity: Tau <sup>2</sup> =	= 0.02; Cl	$ni^2 = 5.$	17, df =	3 (P =	0.16); I <sup>2</sup>	= 42%	6.01		10	100
Test for overall effect	Z = 0.36	5 (P = C)	.72)				0.01	Favours [NRT]	Favours [ENDS]	100

Proportion of participants experiencing adverse events

% of AE =

Recommendations from other countries as reported in the Opinion

**Health Research Board, Ireland** : Electronic cigarette and smoking cessation. An evidence review. Published on 12 October 2020. <u>https://www.hrb.ie/publications/publication/electronic-cigarette-and-smoking-cessation-an-evidence-review/returnPage/1/Accès le 17 janvier 2022</u>. Authors: Joan Quigley, Helen Kennelly, Caitriona Lee, Doireann O'Brien, Michelle Williams, Anne McCarthy, Jean Long

- Seven RCTs met the inclusion criteria for efficacy of e-cigarettes in helping people quit smoking and nine provided data for safety.
- The systematic review and network meta-analysis of e-cigarettes versus therapies usually given for smoking cessation showed that there is no evidence of a difference in effect on incidences of smoking cessation.
- There is a low-level of certainty in these results due to low successful event rates and high rates lost to follow-up in all studies.
- We identified respiratory adverse events, including shortness of breath and cough, that appeared to be higher in e-cigarette users, but in the main, **RCT evidence on adverse events is lacking**.
- The long-term data on e-cigarettes, in line with European Medicines Agency recommendations, are limited for both smoking cessation and adverse events, and further large-scale research using a standardised product to decrease uncertainly at the 1-year timepoint and beyond is needed.

Leone FT, Zhang Y, Evers-Casey S, Evins AE, Eakin MN, Fathi J, Fennig K, Folan P, Galiatsatos P, Gogineni H, Kantrow S, Kathuria H, Lamphere T, Neptune E, Pacheco MC, Pakhale S, Prezant D, Sachs DPL, Toll B, Upson D, Xiao D, Cruz-Lopes L, Fulone I, Murray RL, O'Brien KK, Pavalagantharajah S, Ross S, Zhang Y, Zhu M, Farber HJ. Initiating Pharmacologic Treatment in Tobacco-Dependent Adults. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2020 Jul 15;202(2):e5-e31. doi: 10.1164/rccm.202005-1982ST. PMID: 32663106; PMCID: PMC7365361.

- Question 4: For Tobacco-Dependent Adults in Whom Treatment Is Being Initiated, Should Treatment Be Started with Varenicline or an Electronic Cigarette?
- For tobacco-dependent adults in whom treatment is being initiated, we suggest varenicline over electronic cigarettes (conditional recommendation, very low certainty in the estimated effects). Remarks: The recommendation's strength reflects very low certainty in the effects used to derive the recommendation. After our evidence synthesis, new evidence emerged regarding serious adverse effects of electronic cigarettes. If these serious adverse effects continue to be reported, the strength of the recommendation should be reevaluated. Note that this recommendation is intended for treatment of tobacco dependence under the supervision of a clinician; it should not be extrapolated to unsupervised treatment or recreational use.

US Preventive Services Task Force, Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, Donahue K, Doubeni CA, Epling JW Jr, Kubik M, Ogedegbe G, Pbert L, Silverstein M, Simon MA, Tseng CW, Wong JB. Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2021 Jan 19;325(3):265-279. doi: 10.1001/jama.2020.25019. PMID: 33464343.

The USPSTF concludes that the evidence on the use of e-cigarettes for tobacco smoking cessation in adults, including pregnant persons, is insufficient, and the balance of benefits and harms cannot be determined. The USPSTF has identified the lack of well-designed, randomized clinical trials on e-cigarettes that report smoking abstinence or adverse events as a critical gap in the evidence. **United States Public Health Service Office of the Surgeon General**; National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. Smoking Cessation: A Report of the Surgeon General [Internet]. Washington (DC): US Department of Health and Human Services; 2020. PMID: 32255575.

 E-cigarettes, a continually changing and heterogeneous group of products, are used in a variety of ways. Consequently, it is difficult to make generalizations about efficacy for cessation based on clinical trials involving a particular e-cigarette, and there is presently inadequate evidence to conclude that e-cigarettes, in general, increase smoking cessation. WHO report on the global tobacco epidemic, 2021: addressing new and emerging products: executive summary 17 August 2021 https://www.who.int/publications/i/item/9789240032842

• The focus of this report, addressing new and emerging products, charts a new threat to tobacco control. **ENDS are increasingly** available in many countries along with other novel products like heated tobacco products and nicotine pouches. As they emerge and rapidly evolve, these products can be difficult to characterize and therefore bring with them many regulatory challenges. At the same time, the tobacco and related industries behind these newer products pedal misinformation campaigns, marketing them as "clean", "smokefree" or "safer", and claim they are effective cessation aids. By doing so, these industries attempt to appear part of the solution to the tobacco epidemic, as opposed to instigators and perpetrators of the epidemic.

The European Commission and its Scientific Committee on Health, Environmental and Emerging Risks (SCHEER), final Opinion on electronic cigarettes. https://health.ec.europa.eu/system/files/2022-08/scheer\_o\_017.pdf

 Regarding the role of electronic cigarettes in cessation of traditional tobacco smoking, the SCHEER concludes that there is weak evidence for the support of electronic cigarettes' effectiveness in helping smokers to quit while the evidence on smoking reduction is assessed as weak to moderate. https://solidarites-sante.gouv.fr/prevention-en-sante/addictions/produits-de-vapotage-cigaretteelectronique/article/recommandations-concernant-l-usage-des-produits-de-vapotage-cigarette 26/9/2022

 Recommandations concernant l'usage des produits de vapotage / cigarette électronique





Specific website for general reporting of symptoms and health disorder occuring during and after use.

# Merci de votre attention

